Claim 37 (new). The method of Claim 36 wherein the mucoretentive composition further comprises 0.005% to about 3.0% of citric acid or a salt thereof.

Claim 38 (new). The method of Claim 36 wherein the mucoretentive composition is not further diluted with any liquid prior to administration and the level of colloidal silica is from about 3% to about 15%, by weight of the mucoretentive composition.

Claim 39 (new). The method of Claim 36 wherein the colloidal silica has a mean particle size of less than about 1 micron.

Claim 40 (new). The method of Claim 36 wherein the colloidal silica is colloidal silicon dioxide.

Claim 41 (new). The method of Claim 40 wherein the colloidal silicon dioxide is selected from the group consisting of fumed silicon dioxide, precipitated silicon dioxide, coacervated silicon dioxide, gel silicon dioxide and mixtures thereof.

REMARKS

Claims 30-35 have been cancelled. New Claims 36-41, submitted herewith, are pending in the present application. No new matter has been added by these newly presented claims.

35 U.S.C. Section 102 Rejection

The Examiner has rejected Claims 30 and 33, relating to a method of providing a mucoadhesive coating to the mucosa of the esophagus, stomach and small intestine by swallowing a composition comprising colloidal silica, as being anticipated by the German product "Silicol", manufactured by Saguna GmbH, and by a "Silicol" advertisement submitted by Applicant in the Information Disclosure Statement of October 12, 1999. Applicant has cancelled Claims 30-35. Applicant respectfully traverses the rejection by the Examiner, as it may apply to the newly presented claims.

Anticipation under 35 U.S. C. §102 (a) or (b) requires disclosure of every element of the claims under consideration in a single prior art reference. *See Alco Standard Corp. v.*

TVA, 1 U.S.P.Q.2d 1337, 1341 (Fed. Cir. 1986). Neither the "Silicol" product, nor the "Silicol" advertisement relied upon, teach every element of the present invention. Specifically, these references do not disclose a method of providing an active agent to the mucosa of the esophagus, stomach and/or small intestine. Further, the references do not disclose the step of administration by swallowing a mucoretentive composition that comprises both colloidal silica and a pharmaceutical active(s), as required by the present invention. Therefore, the present invention is not anticipated by "Silicol". Applicant respectfully asks for removal of the rejection based on 35 USC §102.

35 U.S.C. Section 103(a) Rejection

The Examiner has rejected Claims 30-35 as being obvious in light of "Silicol". However, obviousness under 35 USC §103 requires that every claim element be taught or suggested by the prior art. *See MPEP 2143.03; In re Royka 490 F.2d 981, 180 USPQ 580 (CCPA 1974).* Applicant has cancelled Claims 30-35. Applicant asserts that "Silicol" alone does not render the present invention obvious, as "Silicol" does not teach each and every element of the newly presented claims.

The Examiner has also rejected Claims 30-35 as being rendered obvious by "Silicol" in light of WO 98/48814 to Banning *et al* (hereinafter referred to as "Banning"). It is well settled that to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either within the cited reference or within the knowledge generally available to one of skill in the art, to modify or combine the references to reach the present invention. *See In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See also MPEP 706.02(j) and MPEP 2142.* The mere fact that the prior art may be modified as suggested by the Patent Office does not make the modification obvious unless the prior art suggests the desirability of the modification. *See In re Fritch*, 972 F.2d 1260, 23 USPQ 2d 1780 (Fed. Cir. 1992); MPEP 2144.08. Applicant has cancelled Claims 30-35 and submits that one of skill in the art would not be motivated to combine the references cited by the Examiner to achieve the newly presented method claims.

The present invention is directed to a method of administering a pharmaceutically acceptable active agent to the mucosal tissue of the esophagus, stomach and small intestine by swallowing a composition comprising colloidal silica and an active agent. The colloidal silica containing compositions utilized by the present invention are mucoadhesive. That is, the composition adheres to the mucosa of one of the mucosal epithelia. However, in addition

to being mucoadhesive the compositions are also mucoretentive. Thus, the composition upon adhering to the mucosa provides resistance to peristalsis, as well as resistance to the washing and dissolving forces of the fluids of the gastrointestinal (hereinafter "GI") tract. Where a pharmaceutically acceptable active agent is present, sustained retention and sustained release of the active agent to the GI tract, specifically the esophagus, stomach and small intestine, is achieved by the present method.

"Silicol" is a gel consisting only of silicic acid and water. When used internally it forms a protective coating on the gastric and intestinal mucosa. Neither the "Silicol" product nor the accompanying advertisement relied upon by the Examiner, teaches or suggests that the addition of a pharmaceutical active to the compositions taught therein. Thus, each and every element of the present invention is not suggested or taught by "Silicol", specifically, a method of administering an active agent to the mucosa of the esophagus, stomach and small intestine is not taught or suggested by "Silicol" alone.

In addition, there is no motivation to combine the references cited by the Examiner, i.e. "Silicol" and Banning. "Silicol" and the accompanying advertisement not only lack the teaching or suggestion that the addition of an active agent would be advantageous, but the advertisement essentially teaches away from such a modification at Page 2 of the translation provided. The advertisement states, "it should be noted that [the Silicol gel] must be taken at least 1h[our] before or after the intake of medications because Silicol gel may weaken their effect." Thus, one of skill in the art, upon review of this reference, would not be motivated to combine "Silicol" gel with a pharmaceutically acceptable active agent because the reference ostensibly suggests that such a combination might reduce the effectiveness of the active.

Likewise, Banning provides no motivation to one of skill to combine the cited references. Banning relates to compositions comprising sodium alginate and alkali metal bicarbonate and the use of such compositions for the treatment of reflux esophagitis, gastritis, dyspepsia or peptic ulceration and the use of such compositions as targeted delivery or sustained release compositions. The reference does teach that compositions therein have a mucoadhesive property and, thus, are useful for targeted delivery and/or sustained release of pharmaceutically active ingredients. However, there is no suggestion that colloidal silica would be an adequate replacement for the sodium alginate and alkali metal bicarbonate combination taught therein or, more simply, that colloidal silica containing compositions would be useful for delivering pharmaceutical actives to the GI tract mucosa.

Based on the foregoing, Applicant asserts there is no motivation for one of skill in the art to modify or combine the references cited by the Examiner to achieve the present invention.

CONCLUSION

Based on the above amendments, arguments and facts, all rejections or objections are traversed or avoided. Applicants respectfully request withdrawal of all rejections and allowance of all the claims.

Respectfully submitted for
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